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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,498	04/05/2001	Jinhua Xiang	IOWA:030US/GNS	6829

7590 11/20/2002

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EXAMINER	
WINKLER, ULRIKE	
ART UNIT	**PAPER NUMBER**
1648	10

DATE MAILED: 11/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/828,498	XIANG ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *12-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-11* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6, 7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election without traverse of Group I in Paper No. 9 is acknowledged. Claims 1-11 are under consideration in the instant office action.

Sequence listing

Applicant's CRF and paper sequence listing have been entered.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 6 and 7, is attached to the instant Office Action.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited on Applicant's IDS form 1449, Paper Nos. 6 and 7 or by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claim 5 is objected to because of the following informalities: The claim is objected to because it is dependent on a rejected claim. SEQ ID NO: 1 is free of the prior art of record. Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 6-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is drawn to an isolated and purified nucleic acid molecule that encodes an infectious GBV-C. According to the specification (page 6, lines 8-20) an "infectious nucleic acid" is defined as a full-length cDNAs or RNA transcript, which is infectious in cell culture. While an "isolated and purified" (paragraph spanning page 6-7) is defines as a nucleic acid molecule which is not part of an intact GBV-C virus. A cDNA clone made from the full-length or a less-than full-length transcript is also contemplated within the scope of the invention. The nucleic acid molecule encoding GBV-C may contain a contiguous nucleic acid sequence encoding one or more GBV-C genes and regulatory regions and be of the following lengths: 10-12000 nt. (see paragraph spanning page 20-21). The claim is not clear because it can be interpreted in two different ways:

(1) the claim can be interpreted to require full-length cDNA and RNA transcript which according to applicant (page 6, lines 8-20) are different that those described by others because the instantly described infectious cDNA GBV clone is able to replicate *in vitro*; or

(2) the claim can be interpreted as being less than a full-length clone and requiring anywhere from 10-12000 nt.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-4 and 6-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an infectious full-length clone of GBV-C set out in SEQ ID NO:1, does not reasonably provide enablement for an infectious nucleic acid that is less-than or greater-than the full-length clone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Instant claims are evaluated for scope of enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims. The Wands factor analysis, such an analysis does not need to specifically enumerate (points 1-8) but only needs to have a select few of the factors discussed in a rejection.

The nature of the invention is an infectious GBV-C nucleic acid molecule and infectious nucleic acid molecule that comprises a heterologous nucleic acid which encodes a mammalian polypeptide and/or a promoter. The specification provides the following working example, they have shown that the cell culture supernatant from a full-length infectious GBV-C clone (SEQ ID NO:1) contains infectious virus. This was determined by incubating the supernatant with new

uninfected cells (see example 4) and observing signs of infection. The description of a single example which utilizes the full-length clone does not provide sufficient guidance to make infectious clones that may be smaller or larger in size. The unpredictability in the art is determining what size of heterologous sequence can be inserted into the GBV clone while maintaining the ability to be infectious. Increasing the size of the nucleic acid molecule will risk that the molecule will not be able to be packed into a particle. The prior art has shown that the structural proteins can be removed and heterologous sequences can be inserted into the flavivirus, these constructs will allow for the replication of the nucleic acid but they do not produce particles and are thereby not infectious (Pang et al. BMC Microbiology, 1999, see discussion 1st paragraph). The relative skill of those in the art is high. Therefore, without specific guidance or direction and /or working examples, one of ordinary skill in the art would not be able to reproducibly practice the entire scope of the invention as claimed, without undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 6, 7 and 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (U.S. Pat. No. 5,856,134, see IDS).

The instant invention is directed to an isolated and purified nucleic acid molecule encoding a GBV-C virus. The nucleic acid molecule can be RNA or DNA (claims 2 and 3) and the nucleic acid is about 9.4 kilobases (claim 4) in length. The nucleic acid molecule contains heterologous sequences (claims 6 and 7) which include promoters (claims 9-11). Because the claims can be interpreted two ways (see 112 2nd paragraph rejection above), for purposes of the instant rejection the isolated and purified nucleic acid is interpreted as sequences that can be less than full-length GBV-C.

Kim et al. disclose the entire coding region of two hepatitis-G virus DNA clones which are 9.4 kilobases in size (see SEQ ID NOs: 14 and 182). Genomic RNA was extracted (isolated and purified) from purified virions (see column 54, lines 40-52). The reference further discloses the expression and purification of HGV virus protein using a GST fusion construct with a pGEX vector in *E. coli.* (see Example 7), the plasmid contains a heterologous nucleic acid sequence and a promoter for the expression of the construct in a prokaryotic host. Therefore, the instant invention is anticipated by Kim et al.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Xiang et al. (Journal of Virology, 1998, see IDS).

The instant invention is directed to an isolated and purified nucleic acid molecule encoding a GBV-C virus, the isolated nucleic acid is an RNA molecule. Because the claims can be interpreted two ways (see 112 2nd paragraph rejection above), for purposes of the instant

rejection the isolated and purified nucleic acid is interpreted as sequences that can be less than full-length GBV-C.

Xiang et al. disclose RNA extraction (isolation and purification) of HGV RNA from patient plasma samples (see figure 1, and materials and methods). Therefore, the instant invention is anticipated by Xiang et al.

Claims 1-3, 6 and 9-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Pilot-Matias et al. (U.S.Pat. No. 6,156,495).

The instant invention is directed to an isolated and purified nucleic acid molecule encoding a GBV-C virus. The nucleic acid molecule contains heterologous sequences (claims 6 and 7) which include promoters such as T7, T3 or Sp6 (claims 9-11). Because the claims can be interpreted two ways (see 112 2nd paragraph rejection above), for purposes of the instant rejection the isolated and purified nucleic acid is interpreted as sequences that can be less than full-length GBV-C.

Pilot-Matias et al. discloses the production of fusion proteins comprising HGBV virus sequences, the nucleic acids encoding the HGBV virus sequences are inserted into a pSFV1 construct, which contains the heterologous promoter Sp6. The plasmids are linearized before *in vitro* RNA synthesis is performed (see column 45, lines 5-62, and table 5). Therefore, the instant invention is anticipated by Pilot-Matias et al.

Allowable Subject Matter

SEQ ID NO: 1 is free of the prior art of record.

Conclusion

Claims 1-4 and 6-1 are rejected.

Claim 10 is objected to but would be allowable if rewritten in independent form.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ulrike Winkler, Ph.D. 11/18/02